REMARKS

According to the Office Action dated December 28, 2004, claims 7-10, 12-18, and 20-22 are pending and claims 9, and 13 to 16 are withdrawn from consideration.

The Rejection under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claim 12 directed to vaccine formulations is rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. It is argued that, although effective vaccines have been produced for animal models, these vaccines have failed to prove effective in humans. The rejection is further based on the contention that there is no art-accepted animal model for RSV infections in humans. Applicants respectfully disagree because the effectiveness of vaccines that have been produced using the methods of the application have been successfully used in an art-accepted model system, which has been reported in several scientific publications to be predictive of the use in humans.

THE LEGAL STANDARD FOR ENABLEMENT

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

The law also does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims. *See In re Fisher*, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970); *see also In re Wright*, 27 U.S.P.Q.2d 1510 (Fed. Cir. 1993). To be enabled, all the law requires is that the scope of enablement provided by the

specification bear a "reasonable correlation" to the scope of the claims. *Id.* Thus, to support a non-enablement rejection, the Examiner must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate the teaching in the specification across the entire scope of the claims. *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

In addition, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971); MPEP § 2164.02. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.*

Under Section 112, it is not fatal that a certain amount of experimentation may be required to adapt the invention to a specific purpose, provided the experimentation is routine. *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). Moreover, considerable amount of experimentation is permitted if it is merely routine or the specification provides a reasonable amount of guidance and direction to perform such experimentation. *In re Jackson*, 217 U.S.P.Q. 804, 807 (PTO Bd. Pt. App. Int. 1982).

THE CLAIMED VACCINES ARE ENABLED

Karron et al., 1997, Journal of Infectious Diseases 176:1428-1436 ("Karron," Exhibit A) show a correlation between the chimpanzee model system and studies performed in humans for two different cold-passaged, temperature-sensitive candidate vaccines. As in chimpanzees, the vaccine candidates were immunogenic in RSV-seronegative children (Karron, at page 1432, right column). Further, an increase in attenuation in chimpanzees was shown to correlate with an increase in attenuation in humans (Karron at page 1433, right column, first full paragraph, fist sentence). The more attenuated virus, *cpts*530/1009 in chimpanzees was also more attenuated in humans (compare Table 1 and Table 2). Thus, the relative order of attenuation in chimpanzees was identical to the relative order of attenuation in clinical studies (Karron, at page 1434, right column, first full paragraph).

Applicants point to section 2164.02 of the M.P.E.P.:

> "[...] if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model

does not correlate. . . . A rigorous or an invariable exact correlation is not required . . . ."

Karron clearly demonstrates that such a correlation exists between the chimpanzee model system for RSV infections and RSV infections in humans. Thus, contrary to the Examiner's assertion, the chimpanzee model system provides more than relevant information. For example, if a vaccine candidate is more attenuated in chimpanzees than a previously tested vaccine candidate, it can be predicted that this vaccine candidate will also be more attenuated in humans compared to the previously tested vaccine candidate.

Sibal and Samson, 2001, ILAR J. 42(2):74-84 ("Sibal," Exhibit B), states at page 78, left column, lines 4-7, that chimpanzees are the "model of choice for studying RSV disease."

Further, a correlation between data obtained in chimpanzees and in humans has been shown in Wright et al., 1982, Infection and Immunity 37(1):397-400 ("Wright," Exhibit D). Wright describes the attenuated phenotype of RSV *ts*-2 in humans. RSV *ts*-2 had previously been shown to be attenuated in animal model systems, such as chimpanzees (see Abstract, lines 6-8). Thus, there is clearly a correlation between the virulence of RSV in chimpanzees and the virulence of RSV in humans. Although some fine-tuning may be necessary to obtain a vaccine optimal for human use, Applicants assert that such fine-tuning would not constitute undue experimentation because an animal model to assess the degree of attenuation of the virus does exist. In view of the existing correlation between the degree of attenuation in chimpanzees and the degree of attenuation in humans, Applicants assert that it cannot be said that there is a lack of predictability in the art of RSV vaccines. Combining the existing predictability in the art with the guidance provided in the present specification, the skilled artisan would be fully enabled to make and use the claimed vaccines.

Teng et al., 2000, Journal of Virology 74(19): 9317-9321 ("Teng," cited previously) shows that the vaccines taught and claimed in the present application can be successfully used to protect chimpanzees from RSV infection. Teng tested the protective efficacy of recombinant RSV with an inactivated NS1 or M2-2 gene (designated rA2ΔM2-2 and rA2ΔNS1, respectively) in the upper and lower respiratory tracts of chimpanzees. Attenuation and immunogenicity of rA2ΔM2-2 and rA2ΔNS1 are shown in Table 1 at page 9319 of Teng and protection against challenge with wild type RSV is demonstrated by the data shown in Table 2 at page 9319 of Teng.

In response to Applicants reference to Teng, the Examiner refers to page 9320 of Teng and alleges that it teaches that the finding in chimpanzees do not directly carry over to humans. First, the only proposition found in Teng relating to chimpanzees as a model system is that an ultimate determination of a vaccine's suitability in 1- to 2- month-old infants has to be done by clinical trials (see page 9320). This should not be an obstacle to patentability because, as stated above, in order to meet the enablement requirement, an exact correlation is not required (M.P.E.P. 2164.02). First, clinical trials will always be required by the FDA, regardless of the correlative nature of any animal model used. Further, one could dispense with clinical trials only if there was a 100% correlation between the model system and use in humans, *e.g.*, between RSV infections in chimpanzees and RSV infections in humans; such a rigorous correlation between a model system and humans would permit to go directly from the model into humans without further clinical trials. Such a rigorous correlation, however, is not required for patentability. Thus, although clinical trials will still be required, the data obtained in chimpanzees are still sufficiently predictive of the suitability of a vaccine in humans, which is all that is required to meet the enablement requirement.

Further, the Examiner refers to the section of Teng's discussion where it is stated that a vaccine candidate was insufficiently attenuated in RSV-naïve infants and overattenuated RSV-experienced adults to support the contention that there is no correlation between the results obtained in chimpanzees versus results obtained in humans. This statement relates to a vaccine candidate that was derived from a temperature sensitive mutant, *cpts*248/404, and not to vaccine candidates that were derived from the recombinant deletion mutants. Even so, this candidate vaccine had been found infectious, immunogenic, and protective against a second vaccine dose (see Teng at page 9317, left column, third full paragraph)—*i.e.*, all that would be required for a vaccine. Further, simply because different target populations for a vaccine (RSV-naïve infants and RSV-experienced adults) may have different requirements it does not mean at all that the chimpanzee model system is not predictive. As discussed above, the relative order is still the same; a vaccine candidate for use in RSV-naïve infants would have to be more attenuated in the chimpanzee model system than one that would be used for adults.

Similarly, the reliance by the Examiner on the statement in Crowe *et al.*, Virus Res. 59:13-22 ("Crowe," cited in the Office Action of December 28, 2004) that the level of attenuation in humans can only definitely be determined in humans sets the bar for

patentability too high. A model system that would suffice for patentability purposes need to correlate with human use, there is no requirement that it renders human studies unnecessary. Further, Crowe itself states at page 20, that "previous studies have identified a strong correlation between the relative level of replication of attenuated strains in rodents or chimpanzees with that in human infants . . . ."

Per Merriam-Webster Online, a vaccine is defined as "a preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms that is administered to produce or artificially increase immunity to a particular disease" (Exhibit C). That a vaccine that has been generated using the teachings of the present application having these properties has been shown in Teng for chimpanzees, an art-accepted model.

The Examiner further contends that the art shows the difficulty in balancing attenuation and immunogenicity of a vaccine candidate. As discussed in the Legal Standard section, a considerable amount of experimentation is permitted if the experimentation is merely routine or the specification provides a reasonable amount of guidance and direction to perform such experimentation. In re Wands, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). In re Jackson, 217 U.S.P.Q. 804, 807 (PTO Bd. Pt. App. Int. 1982). Any person skilled in the art of molecular biology can construct the recombinant viruses according to the teachings of the specification for use in vaccines by use of knowledge common in the art. Methods for testing these vaccine are merely routine and are readily available to the skilled artisan. Thus, the skilled artisan would be able to determine which of the recombinant viruses once administered as a vaccine would increase immunity to RSV infections when administered as a vaccine without undue experimentation.

Claims 7, 8, 10-12, 17, 18, and 20 to 22 directed to genetically manipulated, infectious paramyxoviruses and vaccine formulations, respectively, are rejected under 35 U.S.C. 112, first paragraph, as allegedly being non-enabled. In particular, the Examiner that the specification fails to provide sufficient guidance towards operative embodiments. The Examiner further contends that the claims are not enabled because there is no obvious correlation between the structure of modifications in the viral genome and the operability of the composition. Applicants respectfully disagree because there is ample guidance in the specification for how to modify the viruses and how to identify infectious, replication-competent viruses from among the genetically manipulated viruses.

THE LEGAL STANDARD

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. U.S. v. Telectronics Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well know in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. See Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." Phillips Petroleum Co. v. United States Steel Corp., 673 F. Supp. 1278, 1291 (D. Del. 1991); see also DeGeorge v. Bernier, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. Fields v. Conover, 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re* Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt*, 190 USPQ 214 (CCPA 1976), at 218-219:

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, ... then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act. *Id.* at 219.

THE INSTANT SPECIFICATION PROVIDES AMPLE GUIDANCE TO THE SKILLED ARTISAN FOR MAKING AND USING THE CLAIMED VIRUSES

First, Applicants wish to clarify a misunderstanding that seems to have arisen in connection with the quote from *Angstadt* (cited immediately above). The Examiner seems to have read this quote to mean that "reasonable certainty before performing" an experiment is required to fulfill the enablement required. The quote, however, stands for the exact opposite proposition that reasonable certainty is not required because otherwise "*all* 'experimentation' is "undue," since the term 'experimentation' implies that the success of the particular activity is *uncertain.*" (emphasis in original). That the specification should provide the skilled artisan with reasonable certainty before performing the experiment whether the claimed product will be obtained is the position taken by the dissent and is therefore not the legal standard. *Id.* at 222. Rather, as set forth *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)):

> " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' "

Thus, all that is required is a reasonable amount of guidance with respect to the direction of the experimentation; reasonable certainty with regard to the outcome of the experimentation is not required.

Guidance with respect to the direction of the experimentation is provided throughout the specification. First, the specification provides teachings of where in the genome of the recombinant viruses modifications can be introduced. For example, section 5.4, beginning at page 20, teaches multiple targets for modifications that would result in attenuation of the virus. It is taught that modifications can be introduced into the coding sequences of the F protein, the G protein, the NS1 protein, the NS2 protein, the M1 open reading frame, the M2

open reading frame, the N protein, the P protein, or the L protein. Alterations of non-coding regulatory regions to down-regulate, *e.g.*, the transcription of a gene is discussed at page 22, lines 8-21. Modifications of viral surface antigens to reduce the binding affinity of the viral antigen is taught at page 23, lines 19-34. Alterations that affect viral enzyme activity are taught at page 24, lines 5-15. Moreover, at page 38, lines 29-34, and page 38, lines 4-15, of the specification as filed, it is described that certain genes of RSV can be translocated from one position in the RSV genome to another to take advantage of the 3' to 5' gradient in virus gene expression to accomplish viral attenuation. A detailed description of how the viral polymerase can be modified to achieve attenuation of the virus can be found in section 5.4.1., beginning at page 24 of the specification as filed. Another type of mutation that is taught by the specification as filed are mutations in the cleavage site of the F protein to reduce the efficiency of its cleavage and thereby reduce virulence (see, *e.g.*, page 40, lines 6-14). Those types of mutations are only a few examples of strategies that are taught by the specification as filed for obtaining the claimed viruses. Moreover, the specification as filed discloses many different mutant viruses that were actually made and analyzed. Substitution of the open reading frames of the G and F genes of one subgroup of RSV with the open reading frames of the G and F genes of another subgroup of RSV is described in section 8.1 beginning at page 49 of the specification as filed. Mutants of the L gene are described in section 9 at page 55 of the specification as filed. The effects of these mutants on the viability of the viruses are described in section 9.3.1 at page 58 to section 9.3.3 at page 59, and in Table II at page 62. These illustrative mutations and their effects on virus viability provide guidance for the skilled artisan to make and use the claimed viruses. Mutant virus without the SH and/or M2-2 genes are described in section 10 beginning at page 59.

The specification further provides guidance as to the identification of recombinant viruses that have the properties recited in the claims. With respect to vaccine claims, the specification teaches, *e.g.*, at page 21, lines 24-28, that an attenuated virus exhibits a slower growth rate. Tests for the growth rate of a virus are readily available to the skilled artisan and are merely routine in the art. The specification further teaches how mutant viruses can be generated and how the replication competent, infectious viruses can be identified. Applicants even describe a strategy to facilitate the identification of infectious and replicating viral mutants. In section 9.2, beginning at page 57, Applicants describe how the functionality of L

gene mutants can be tested using the "minigenome" system. This system can be used to exclude mutants that would result in lethality of the virus caused by inactivity of the L gene.

Thus, the instant specification, together with information which was readily available to the skilled artisan at the time the instant application was filed, provides a disclosure that fully enables the claimed viruses. Accordingly, Applicants respectfully request that the rejection of claims 7, 8, 10-12, 17, 18, and 20-22 under 35 U.S.C. 112, first paragraph, be withdrawn.

The Examiner further contends, that, because there is no obvious correlation between the structures of the modifications and their effect on the virus, there would have been no or little certainty as to the operability prior to the experimental determination. As discussed above, there is no legal requirement that there be certainty before an experiment is performed. Rather, all that is required is reasonable amount of guidance with respect to the direction of the experimentation. Further, the specification teaches how the structure of certain modifications would affect the properties of the virus. For example, at page 22, lines 3-7, of the specification, it is taught that non-coding regulatory regions can be modified to obtain attenuated viruses. Further, at page 23, lines 15-23, it is taught that modifications can be introduced into the viral surface antigens to interfere with the binding affinity of the virus to the host cell. Further, at page 24, lines 3-27, it is taught that viral enzymes can be modified to reduce their activity and thereby attenuate the virus.

The Examiner distinguishes the present situation from *Angstadt* by contending that there is a structure-function relationship between the catalysts that were the subject matter in *Angstadt*. First, Applicants respectfully point out that, even assuming *arguendo* there was such a relationship in *Angstadt*, any such correlation was not the reason for the decision of the court. Rather, the court held the claims to be enabled because the skilled artisan "would merely read appelants' specification for directions how to make and use the catalyst complex . . . and could then determine whether hydroperoxides are, in fact, formed." *Id.* at 218. Second, as discussed above, Applicants own specification teaches modifications of the viral genome and their expected effects on the virus.

Claims 7, 8, 10, 12, 17, 18, and 20 directed to genetically manipulated, infectious paramyxoviruses and vaccine formulations, respectively, are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement.

THE LEGAL STANDARD

The test for sufficiency of written description is whether the disclosure of the application 'reasonably conveys to the artisan that the inventor had possession' of the claimed subject matter. *In re Kaslow*, 707 F.2d 1366, 1375, 217 U.S.P.Q. (BNA) 1089, 1096 (Fed. Cir. 1983); accord *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563; *see also*, *Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575, 227 U.S.P.Q. (BNA) 177, 179 (Fed. Cir. 1985). The Court of Appeals for the Federal Circuit has repeatedly considered the written description requirement and consistently found that exacting detail is not necessary to meet the requirement:

> If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if [not] every nuance of the claims is explicitly described in the specification, the adequate written description requirement is met.
> *In re Alton*, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

The criteria for determining sufficiency of written description set forth in Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶ 1, "Written Description Requirement" ("the Guidelines") (published in the January 5, 2001 Federal Register at Volume 66, Number 4, p. 1099-1111), specifies that:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a) above), reduction to drawings (see (1) (b) above), or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see (1)(c), above). *Id.* at p. 1106, column 3, *l.* 13-29.
>
> What constitutes a 'representative number' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. M.P.E.P. 2163(II)(A)(3)(a)(ii) and M.P.E.P. 2163.05(I).

Where the specification discloses any relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics sufficient to allow a skilled artisan to recognize the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, is misplaced.

Furthermore, in accordance with the Guidelines, what is conventional or well known to one of skill in the art need not be disclosed in detail, and, where the level of knowledge and skill in the art is high, a written description question should not be raised.

THE INSTANT SPECIFICATION PROVIDES SUFFICIENT WRITTEN DESCRIPTION FOR THE CLAIMS

The Examiner argues that because it is uncertain whether viruses with modifications that were not actually made are operative, Applicants were not in possession of the claimed viruses. Applicants respectfully disagree because, as discussed above under enablement, the specification specifically teaches numerous examples of how to identify the operative viruses from among the mutated viruses. Applicants disclose the rescue of a non-segmented negative-stranded RNA virus from a cDNA encoding the viral genome, thereby making non-segmented negative-stranded RNA viruses accessible to recombinant DNA technology (see, *e.g.*, Example 6, beginning at page 30 of the specification as filed). As described throughout the specification, recombinant DNA technology can be used to genetically modify the viral genome and generate infectious, replicating viruses. Further, the specification teaches that the viruses be infectious and replicating and that this feature can be tested, *e.g.*, by plaque formation (see, *e.g.*, page 59, lines 7-10, of the specification as filed).

The Examiner further cites *In re Smythe and Shamos*, 178 U.S.P.Q. 279 (Cust. & Pat. App. 1973) to support the conclusion that the present specification fails to provide a sufficient number of working examples to meet the written description requirement. The issue in *Smythe* was whether the description by teaching "air or other gas as a segmentizing medium to separate the liquid samples [in the claimed apparatus]" provided written description support for the claim term "fluid." *Id.* at 284. The court held that it did because it "would naturally occur to one skilled in the art reading the description . . . that in this invention the characteristics of a fluid are what make the segmentizing medium work in this invention." *Id.* Thus, *Smythe* stands for the proposition that the disclosure of a limited number of species may provide sufficient written description support for a later claimed

genus or combination. Applicants respectfully point out that the specification as originally filed does provide literal support for the claimed paramyxoviruses, see, *e.g.*, page 30, lines 13-16. Thus, contrary to the Examiner's assertion, under *Smythe* the present application does meet the written description requirement.

The Examiner further contends that Applicants' specification fails to teach a correlation between the functional and structural characteristics of the claimed viruses. The Examiner relies on *University of California v. Eli Lilly*, 43 U.S.P.Q. 1398 (Fed. Cir. 1997) for the proposition that such a correlation is required. In *Eli Lilly*, the court held that claims that were directed to mammalian insulin cDNAs were invalid for failing to meet the written description requirement where the only insulin cDNA disclosed was the cDNA encoding rat insulin. The court held: "a generic statement such as 'vertebrate insulin cDNA' or mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function." *Id.* at 1406. Thus, the present application can be readily distinguished from *Eli Lilly*; the present claims set forth not only a functional limitation, *i.e.*, that the virus is replication competent and infectious, but also a structural limitation, *i.e.*, that the virus is a virus of the paramyxoviridae family and that the viral genome comprises a certain modification. Further, as discussed above in the enablement section, the present application more than adequately describes numerous examples of mutations that can be made to achieve the presently claimed invention.

Accordingly, the rejection of claims 7, 8, 10, 12, 17, 18, and 20 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement, should be withdrawn.

The Rejection Under 35 U.S.C. § 103 Over Murphy Should Be Withdrawn

Claims 18 and 20-22 were rejected under 35 U.S.C. § 103 over U.S. Patent 5,993,824 to Murphy *et al.* ("Murphy"). Murphy is cited against the presently pending claim using its 102(e) date of July 15, 1997. However, the priority date of the present application of September 30, 1994 predates the 102(e) date of Murphy. It is alleged that claims 18 and 20-22 are not entitled to priority benefit of priority application serial no. 08/316,439 (the "'439 Priority Application") and that therefore Murphy is prior art against claims 18 and 20-22.

Applicants respectfully disagree because claims 18 and 20-22 are supported in the '439 Priority Application.

In particular it is argued that the '439 Priority Application lacks support for any substitution or deletion of any RSV open reading frame. Applicants respectfully disagree. For example, at column 43, lines 6-10 of U.S. Patent 5,840,520, which issued from the '439 Priority Application, insertion of the CAT gene between the leader and trailer sequences of RSV is described. The insertion of the CAT gene into the RSV miniature genome is a substitution of all RSV open reading frames with the CAT open reading frame.

Further, at column 16, lines 58-62, of U.S. Patent 5,840,520, which issued from the '439 Priority Application, it is described that foreign gene sequences can be inserted into the viral segments of influenza by complete replacement of the viral coding region with the foreign gene sequence, *i.e.*, a substitution of a complete open reading frame. At column 14, lines 45-52, it is discussed that the principles discussed in the patent for influenza may be analogously applied for respiratory syncytial virus, an example of the paramyxoviridae.

Further, insertion of the F gene and/or the G gene of one subgroup of respiratory syncytial virus into the genome of a different subgroup of respiratory syncytial virus in place of, or in addition to, the F gene and/or the G gene of the recipient genome are described at column 47, lines 30-36 of U.S. Patent 5,840,520, which issued from the '439 Priority Application.

Thus, claims 18 and 20-22 are entitled to the priority date of the '439 Application and Murphy is not prior art under 35 U.S.C. § 102(e). Applicants therefore respectfully request that the rejection under 35 U.S.C. § 103 over Murphy be withdrawn.

Conclusion

Applicants respectfully request that the present remarks and amendments be entered and made of record in the instant application. An allowance of the application is earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

No fee is believed to be required for this response. However, should any fee be due, please charge the required amount to Jones Day Deposit Account No. 503013.

Respectfully submitted,

by: Sebastian Kartzinel (Reg. No. 52,413)

Date June 28, 2005

Laura A. Coruzzi 30,742

Laura A. Coruzzi (Reg. No.)
JONES DAY
222 East 41st Street
New York, New York 10017
Telephone: 212-326-3939